International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

# Remineralisation of Incipient Lesions - A Narrative Review

**Dr. Kalpana Khanoria[1], Dr. Anshu Minocha[2], Dr. Bhanu Pratap Singh[3]**

[1]Final Year Postgraduate Student, Department of Conservative Dentistry and Endodontics, Himachal Pradesh Government Dental College, Shimla, India

[2]Professor, Department of Conservative Dentistry and Endodontics, Himachal Pradesh Government Dental College, Shimla, India

[3]Assistant Professor, Department of Conservative Dentistry and Endodontics, Himachal Pradesh Government Dental College, Shimla, India
Email: *kalpanakhanoria692[at]gmail.com*

**Abstract:** ***Caries is not simply a continuous and unidirectional process of the demineralization of the mineral phase, but a cyclic event with periods of demineralisations and remineralisation of acid ions from the plaque to the advancing front and mineral ions from the advancing front toward the plaque. The remineralization process is a natural repair mechanism to restore the minerals again, in ionic forms, to the hydroxyapatite (HAP) crystal lattice. The focus on caries has recently shifted to the development of methodologies for the detection of the early stages of caries lesions and the use of non - invasive treatment for these lesions. Remineralisation can occur naturally or be induced by therapies. Remineralization of white - spot lesions and carious lesions may be possible with a variety of currently available agents containing fluoride, bioavailable calcium and phosphate, and casein phosphopeptide in - amorphous calcium phosphate, self - assembling peptide.***

**Keywords:** Incipient lesions, Demineralisation, Remineralisation

## 1. Introduction

Worldwide, dental caries contributes 10 times more burden of oral disease than periodontal or any other common oral conditions. Dental caries is a dynamic process resulting from an imbalance between demineralization and remineralization of the dental surface.[1] It begins when bacteria in acidogenic dental plaque-mainly *Streptococcusmutans*, *Streptococcus sobrinus* and *Lactobacillus acidophilus*-ferment carbohydrate in the diet[2] producing organic acids such as lactic, formic, pyruvic, butyric, acetic and propionic acids. These acids act on hydroxyapatite crystals, freeing the calcium and phosphate mineral content and thereby, initiating the process that forms cavity.3 Critical pH is the term given to the highest pH at which there is a net loss of minerals from tooth enamel. The critical Ph for enamel is 5.5 and 6.2 for dentin. Below this Ph, tooth begins to demineralise. The incipient carious lesions represent the earliest phase of tooth decay or demineralisation. This process is generally slow, and periods of demineralization alternate with other periods at an early stage of disease that is when the layer of enamel is intact, and if oral conditions change, the incipient lesion can remineralize.[3]

The remineralization process is a natural repair mechanism to restore the minerals again, in ionic forms, to the hydroxyapatite (HAP) crystal lattice.[4] It occurs under near - neutral physiological pH conditions whereby calcium and phosphate mineral ions are redeposited within the caries lesion from saliva and plaque fluid resulting in the formation of newer HAP crystals, which are larger and more resistant to acid dissolution.[5]

The focus on caries has recently shifted to the development of methodologies for the detection of the early stages of caries lesions and the use of non - invasive treatment for these lesions. Remineralisation can occur naturally or be induced by therapies. Among the available therapies, fluoride (F) –based treatments have the highest level of supporting evidence and the widespread use of fluorides is generally considered the main reason for dental caries reduction in most populations. Remineralization of white - spot lesions and carious lesions may be possible with a variety of currently available agents containing fluoride, bio available calcium and phosphate, and casein phosphopeptide in - amorphous calcium phosphate, self - assembling peptide. The current concept further bridges the traditional gap between prevention, non - invasive and surgical procedures which is just what dentistry needs for the current age.

**Dispensing methods of Remineralising Agents**

Remineralising agents can be incorporated into different products for application. Commonly used vehicles are restorative materials (GIC, COMPOMERS, GIOMERS), pit - and - fissure sealants, dentifrices, chewing gums, and rinses.

**Requirements of an Ideal Remineralisation Material:**

a) Diffuses into the subsurface or delivers calcium and phosphate into the subsurface.
b) Does not deliver an excess of calcium, which might enhance calculus formation.
c) Works at acidic, neutral, and basic pHs.
d) Works in xerostomic patients.
e) Enhances or maintains the remineralising properties of saliva.
f) For novel materials, shows a benefit over fluoride, or establishes a synergistic effect with fluoride to promote remineralisation.

**Indications of remineralisation**

a) An adjunct to preventive therapy for reducing caries in high - risk patients.

b) Reduce dental erosion in patients with gastric reflux or other disorders.
c) To reduce decalcification in orthodontic patients.
d) To repair enamel in cases involving white spot lesions.
e) For fluorosis, before and after teeth whitening and to desensitize sensitive teeth.

**Advantages of remineralisation**

Remineralization treatment, which offers the advantage of being non - invasive, is being increasingly used as a principal tool of minimal intervention dentistry (MID) treatment in managing caries.6Such treatment has several advantages over conventional invasive treatments:

1) It conforms with the recommendations of the World Dental Federation advocating MID);
2) It is a procedure that respects Nature, since biologically caries is formed as a result of the interplay between demineralization and remineralization and "caries demonstrates a dynamic pathology of sequential demineralisation and remineralization"; [7]
3) It may allow treatment not only of incipient enamel lesions in which the surface is relatively intact, but also of lesions that have penetrated to the dentin, especially when caries risks can be controlled at a low level;
4) If the lesions are detected early, non - invasive treatment[8] can be applied long - term in order to suppress caries progression and to promote remineralization;
5) It will promote better general oral health;
6) It is less burdensome for patients mentally, physically and financially.

**Challenges in implementation of remineralisation**

There are several challenges to establishing the clinical effectiveness of remineralization agents:

1) They must demonstrate a benefit over and above an established and highly effective agent, namely, fluoride.
2) They must provide a remineralising benefit in addition to the natural remineralising properties of saliva.
3) The organic constituents of saliva can serve as accelerators and inhibitors of the remineralization process. Teeth are covered by the acquired pellicle, which has been shown to retard remineralization.
4) If sugar - free chewing gum is the delivery vehicle, chewing gum has a major remineralising effect in and of itself, which makes it more challenging to show an additional benefit when using gum as the delivery vehicle.
5) Too much of a good thing could possibly disrupt the mineralization homeostasis of the mouth and favor calculus formation.
6) There may be ingredient compatibility issues. Products are designed to deliver a new agent (i. e., calcium ions) and fluoride simultaneously from single - phase products and may present formulation challenges such as long - term fluoride compatibility.
7) Preclinical models may not necessarily be predictive of clinical performance for these non - fluoride agents and that new agents still require direct clinical validation to ensure efficacy.

**Classification**

Remineralising agents have been broadly classified into the following:

a) Fluorides based remineralising agents
b) Nonfluoride remineralising agents

**Fluoride based remineralisation**

Since the 1980's customary fluoride - based remineralisation was regarded as the benchmark for rendering carious lesions inactive, which was established by the several evidence - based literature.[9] This considerable decrease in caries experience in developed nations from the twentieth century was mainly accredited to extensive utilisation of fluoride products.

Soi et al. have mentioned four mechanisms of action of fluoride.1[0]Fluoride inhibits demineralization as the fluorapatite crystals, formed by reaction with enamel apatite crystals, are more resistant to acid attack compared to HAP crystals. Second, fluoride enhances remineralization as it speeds up the growth of the new fluorapatite crystals by bringing calcium and phosphate ions together. Third, it inhibits the activity of acid producing carious bacteria, by interfering with the production of phosphoenol pyruvate (PEP) which is a key intermediate of the glycolytic pathway in bacteria. And also, the $F^-$ retains on dental hard tissue, the oral mucosa and in the dental plaque to decrease demineralization and enhance remineralization.

The various types of topical fluorides used in dentistry are: Sodium fluoride (NaF), sodium mono - fluorophosphate, stannous fluorides and acidulated phosphate fluoride (APF). All these fluorides are inorganic in nature and are available in the form of solutions, varnishes, foam, gels, dentifrices etc.

Fluoride delivery method

**a) Topical Fluoride**

Professionally applied - neutral sodium fluoride, stannousfluoride, APF gels, varnish
Self applied - dentrifices, mouth washes, flurode gel

**b) Systemically Delivered**

Water fluoridation – community and school water fluoridation
Milk
Salt
Fluoridedrops, lozenges

**Requirement for non - fluoride strategies:**

1) Effect of fluoride seems to be more extensive on smooth - surface caries, but it displays limited efficacy on pit and fissure caries.
2) To avoid the potential for adverse effects (e. g., fluorosis) a high - fluoride strategy cannot be followed.
3) Fluoride toxicity increases with inadequate nutrition.
4) In spite of proving its remineralising efficacy, there is a wide gap when it comes to complete rehabilitation.
5) The anti - fluoride lobby, which is staging pressure, posed certain legal implications when it comes to using fluoride.
6) The availability of fluoride products is still questionable in certain nations.

**Non - fluoride remineralisation:**

1) Biomimetic Regeneration Systems.
2) Agents that deliver calcium and phosphate ions to the tooth surface.
3) Agents that modify the biofilm.
4) Agents that neutralise organic acids.
5) Antimicrobials and antibiotics

**1) Biomimetic Remineralisation of the Dentin and Enamel**

Most of these studies on remineralization were based on the epitaxial deposition of calcium and phosphate ions over existing apatite seed crystallites.[11] According to this concept, remineralization does not occur in locations where seed crystallites are absent particularly in completely demineralized dentin due to the unavailability of seed crystallites in those regions. In this so - called nonclassical particle - based crystallization concept, calcium and phosphate ions are sequestered by biomimetic analogs of non - collagenous proteins involved in hard tissue mineralization into nanoparticles. It then penetrates into the intrafibrillar water compartments of a collagen fibril and undergoes self - assembly and crystallographic alignment to form a metastable crystalline phase. These crystals fuse finally into single apatite crystallites within the zone between the collagen molecules.[11]

a) **Dentine Phosphoprotein - Derived 8DSS Peptides:** 8DSS peptides appear to have a dual mechanism in the mediation of biologically directed mineral deposition. First, they limit the dissolution of Ca2+ and PO4 3– ions from demineralized dentine, and second, they promote the capture of these ions to form new mineral deposits on demineralised enamel.[12]
b) **Self - Assembling P11 - 4 Peptides:** Thisrationally designed peptide self - assembles into hierarchical 3 - dimensional fibrillar scaffolds in response to local conditions such as high ionic strength and acidic pH found in the lesion body. The P11 - 4 fibrillar matrix has a high affinity for Ca2+ ions and acts as a nucleator for de novo HA formation resulting in remineralisation of the lesion body.[13]
c) **Amelogenin:** In vitro studies have shown treatment of enamel lesions with leucine - rich amelogenin peptide reduced lesion depth and allowed biomimetic reconstruction of enamel by promoting linear growth of mature enamel crystals.
d) **Poly (Amido Amine) Dendrimers:** These amelogenin - inspired dendrimers have been referred to as “artificial proteins” as they can mimic the functions of organic matrices in modulating the biomineralization of tooth enamel.
e) **Electrically Accelerated and Enhanced Remineralization:** It utilizes iontophoresis to accelerate the flow of remineralising ions into the deepest part of the subsurface caries lesion. This creates an environment that favours remineralisation of the lesion that then matures to give the repaired lesion optimal hardness and mineral density.

**2) Agents that Deliver Calcium and Phosphate Ions to the Tooth Surface.**

**Calcium Phosphate Compounds:**

Beta TCP: Tricalcium phosphate has the chemical formula Ca3 (PO4) 2, and exists in two forms, alpha and beta. Beta TCP is less soluble than alpha TCP, and thus in an unmodified form is less likely to provide bio - available calcium. It is used in products such Cerasorb®, Bio - Resorb® and Biovision®.

**Functionalised β - Tricalcium Phosphate** It is a smart calcium phosphate system that effectively regulates the diffusion of tooth mineral. The agenda behind functionalising β - TCP was to produce barriers averting the untimely interactions of fluoride - calcium. This permits β - TCP to behave as a targeted low - dose delivery system using dentifrices or mouthwashes as vehicles. Clinical recommendations on employing fTCP products will be premature since there is limited evidence owing to scanty in vitro studies and well - designed randomised controlled trials (RCT)

**Case in phosphor - peptides - amorphous calcium phosphate** (CPP - ACP) CPP stabilize ACP, localize ACP in dental plaque, thereby maintaining a state of supersaturation with respect to tooth enamel, reducing demineralization and enhancing remineralization. The CPPs have been shown to keep fluoride ions in solution, thereby enhancing the efficacy of the fluoride as a remineralising agent. CPP stabilize ACP, localize ACP in dental plaque, thereby maintaining a state of supersaturation with respect to tooth enamel, reducing demineralization and enhancing remineralisation.[14] The CPPs have been shown to keep fluoride ions in solution, thereby enhancing the efficacy of the fluoride as a remineralizing agent.

**Amorphous calcium phosphate:** ACP is a dual chamber fluoride toothpaste which incorporates an unstabilised calcium - phosphate system and separately delivers Ca2+ and PO43 - ions in the oral cavity[135]. It results in the intraoral mixing of Ca2+ and PO43 - on brushing. This is then followed by a rapid deposition of ACP or amorphous calcium fluoride phosphate. These precipitated products have been found to be unsteady, so they change rapidly to a steadier form - HA or fluorhydroxyapatite.

**ACP - filled Composites:** A biologically active restorative material containing ACP as a filler encapsulated in a polymer binder. It releases calcium and phosphate ions into saliva and deposit into tooth structures as an apatitic mineral, which is similar to the HAP found naturally in teeth.

**Dicalcium phosphate dehydrate:** Inclusion of DCPD in a dentifrice increases the levels of free calcium ions in plaque fluid, and these remain elevated for up to 12 h after brushing, when compared to conventional silica dentifrices.

**Bioactive glass:** When in contact with saliva or water, first releases sodium ions. This elevates the pH into the range essential for HAP formation (7.5 - 8.5). The calcium and phosphate are released to supplement the normal levels found in saliva. This increase in ionic concentration,

combined with an increase in pH, causes the ions to precipitate onto the tooth surface and form calcium hydroxycarbonate apatite (HCA) to remineralise the defect and to occlude open tubules.

**Nanomaterials:** These materials are often added to restorative materials as inorganic fillers, such as resin composites to release calcium, phosphate, and fluoride ions for remineralisation of dental hard tissues Nanotechnology helps in treating dental caries by two important approaches. The first approach is the remineralization process, which uses nano - materials with fluoride and calcium releasing ability, namely, calcium phosphate, calcium fluoride, hydroxyapatite, and fluorohydroxyapatite. The second approach involves the administration of antibacterial nanoparticles such as silver, quaternary ammonium polyethylene amine, and zinc oxide. Better outcomes are achieved by the combination of these two approaches.

Calcium Fluoride Nanoparticles
Calcium Phosphate - based Nanomaterials
NanoHAP Particles.

**3) Agents that modify the biofilm**

**Arginine Bicarbonate** Arginine bicarbonate is an amino acid with particles of calcium carbonate, which is capable of adhering to the mineral surface. When the calcium carbonate dissolves, the released calciumis available to remineralise the mineral while the release of carbonate may give a slight local pH rise.

**4) Those neutralizing the bacterial acid**

Other strategies to combat demineralisation include neutralizing bacterial acid using calcium carbonate as plaque pH buffering effect and sodium bicarbonate to provide an alkaline oral environment. Alternatively, calcium containing agents like calcium lactate, calciumglycerophosphate, and calcium phytate can be used. They act by increasing plaque calcium and phosphate level.

**5) Anti - microbials and antibiotics**

Many types of mouth rinse active ingredients have been evaluated for their plaque - reducing effectiveness and ability to reduce mutans streptococci, including chlorhexidine, essential oils, triclosan, cetylpyridinium chloride, sanquinarin, sodium dodecyl sulfate, and various metal ions (tin, zinc, copper).

**Other Remineralising Agents:**

**Polydopamines:** In demineralized dentin, the collagen fibers when coated with polydopamine, remineralization was promoted, which shows that polydopamine binding to collagen fiber act as a new nucleation site that will be favorable for HA crystal growth.

**Natural Products**

1) **Xylitol:** It exerts the anticariogenic effects by the inactivation of *S. mutans* and inhibition of plaque's ability to produce acids and polysaccharides. When consumed as mints or gum, it will stimulate an increased flow of alkaline and mineral - rich saliva from small salivary glands in the palate. Increased salivary flow results in increased buffering capacity against acids and high mineral content will provide the minerals to remineralise the damaged areas of enamel.[15]
2) **PA:** Grapeseed extract contains proanthocyanidin (PA) which is a type of polyphenol. And have anti - inflammatory and antioxidant properties. Proanthocyanidin acts *via* accelerating the conversion of soluble to insoluble collagen. inhibition of glucosyl transferases by PA in turn inhibits caries.[16]
3) **Yogurt Extract:** Milk proteins inhibit demineralisation of enamel by getting adsorbed on the enamel surface. Milk enzymes also plays a role in decreasing the growth of cariogenic bacteria. At acidic pH, calcium ions are released from yogurt and thus helps in remineralisation of enamel.
4) **Hesperidine:** This results in stability of collagen matrix and promotes remineralisation as collagen matrix acts like a scaffold for deposition of minerals.[17]

## 2. Conclusion

The era of preventive and minimally invasive dentistry clearly dictates the need for developing newer approaches to remineralise enamel caries lesions. While fluoride mediated natural repair of early lesions can occur by influencing oral hygiene and diet, this is dependent on variables such as saliva quality and patient compliance.

Non - fluoride remineralization systems are less reliant on such factors and can also significantly improve the structure, aesthetics, and acid resistance of the remineralised lesion. Furthermore, effective non - fluoride remineralising strategies can prevent a non - cavitated lesion from being subjected to a "death spiral of restorations" due to secondary caries at the enamel - restoration interface.

However, a biomimetic strategy for enamel regeneration may well be the future, where organized enamel apatite crystals with r robust attachment to the tooth surface are grown to replace demineralized tissue

## References

[1] Featherstone JD. The continuum of dental caries: Evidence for a dynamic disease process. J Dental Res 2004; 83: c39 - c42
[2] Featherstone JD. Prevention and reversal of dental caries: Role of low level fluoride. Community Dent Oral Epidemiol 1999; 27 (1): 31 - 40.
[3] Barbaria E, Maroto M, Arenas M, Silva CC. A clinical study of caries diagnosis with laser fluorescence system. J Am Dent Assoc 2008; 139 (5) 572 - 79. '
[4] Hemagaran G. Remineralisation of the tooth structure—the future of dentistry. Int J PharmTech Res 2014; 6 (2): 487–493.
[5] Naveena Preethi P, Nagarathana C, et al. Remineralising agent—then and now—an update. Remineralising agent—then and now—an update. Dentistry 2014; 4 (9): 1–5.
[6] FDI World Dental Federation. FDI policy statement on Minimal InterventionDentistry (MID) for managing dental caries: adopted by the General Assembly: September 2016, Poznan, Poland. Int Dent J 2017; 67: 6–7.

[7] Holman L, Thylstrup A, Artun J. Surface changes during the arrest of activeenamel carious lesions in vivo. A scanning electron microscope study. ActaOdontolScand1987; 45: 383–90.
[8] . Nyvad B, Fejereskov O. Scanning electron microscopy of early microbial col - onization of human enamel and root surfaces in vivo. Scand J Dent Res1986; 94: 281–4.
[9] Benson PE, Parkin N, Dyer F, et al. Fluorides for the prevention of early tooth decay (demineralised white lesions) during fixed brace treatment. Cochrane Database Syst Rev 2013; (12): CD003809.
[10] Soi S, Vinayak V, et al. Fluorides and their role in demineralisation and remineralisation. J Dent Sci Oral Rehabil 2013 July–Sep; 19–21.59.
[11] Zhou YZ, Cao Y, et al. Polydopamine - induced tooth remineralisation. AC Appl Mater Interfaces 2012; 4: 6901–6910. DOI: 10.1021/am302041b.
[12] C C Hsu, H Y Chu influence of 8DSS peptide on nano - mechanical behavior of human enamel J Dent Res 2011 Jan; 90 (1): 88 - 92. doi: 10.1177/0022034510381904.
[13] Kirkham, J., Firth, A., Vernals, D., Boden, N., Robinson, C., Shore, R. C., … Aggeli, A. (2007). Self - assembling peptide scaffolds promote enamel remineralization. Journal of Dental Research, 86, 426–430. https: //doi. org/10.1177/15440591070860050.
[14] Reynolds EC. Remineralization of enamel subsurface lesions by casein phosphopeptide - stabilized calcium phosphate solutions.1997; 76: 1587 - 9.
[15] Makinen K. Sugaralcohols. Caries incidence and remineralisation of caries lesions, a literature review. Int J Dent 2010; 981072.
[16] Wu CD. Grape products and oral health. J Nutr 2009; 139 Suppl: 1818S-23S.
[17] Crivelaro de Menezes TE, BotazzoDelbem AC, LourençãoBrighenti F, Cláudia Okamoto A, Gaetti - Jardim E Jr. Protective efficacy of Psidiumcattleianum and Myracrodruonurundeuva aqueous extracts against caries development in rats. Pharm Biol.2010; 48 (3): 300